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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/762,693	07/03/2001	Lewis T. Williams	PP01521.101	7839

7590 03/22/2004

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EXAMINER	
NGUYEN, QUANG	
ART UNIT	**PAPER NUMBER**
1636	

DATE MAILED: 03/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/762,693	WILLIAMS ET AL.	
	Examiner	Art Unit	
	Quang Nguyen, Ph.D.	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-24,26-34 and 36-40* is/are pending in the application.

4a) Of the above claim(s) *1-16,26,30,31,36,38 and 40* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17-24,27-29,32-34,37 and 39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicants' amendment filed on 1/5/04 has been entered.

Claims 1-24, 26-34 and 36-40 are pending in the present application.

This application contains claims 1-16, 26, 30-31, 36, 38 and 40 drawn to an invention nonelected without traverse in Paper No. 9. A complete reply to the final rejection must include cancelation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01. Applicants further elected without traverse the following species: (a) dendritic cell as an antigen presenting cell, (b) neomycin as a selectable marker, (c) cancer cell as the target cell, and (d) IL-2 as the immunomodulatory cofactor.

Accordingly, amended claims 17-24, 27-29, 32-34, 37 and 39 are examined on the merits herein.

Claim Objections

Claim 23 is objected to because the phrase "a polynucleotide encoding least one selectable marker" is not grammatically correct. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Amended claims 28-29, 32-34, 37 and 39 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of activating T cells comprising contacting a T cell with an autologous dendritic cell of claim 27 or a method of killing a cancer cell in a subject comprising administering to the subject an autologous dendritic cell of claim 27, does not reasonably provide enablement for a method of activating T cells or a method of killing a cancer cell in a subject using any genetically modified allogeneic or xenogeneic dendritic cells of claim 27. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims for the same reasons already set forth in the previous Office Action mailed on 7/3/03 (pages 3-6).

Examiner notes that Applicants failed to address the above issue in the Amendment filed on 1/5/04.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Amended claims 17-22, 27-29, 32-34, 37 and 39 stand rejected under 35 U.S.C. 102(e) as being anticipated by Nair et al. (U.S. Patent No. 5,853,719) for the same reasons already set forth in the previous Office Action mailed on 7/03/03 (pages 8-9).

With respect to the elected species, Nair et al. teach a method for producing an RNA-loaded antigen-presenting cell (APC) including a dendritic cell by introducing into an APC tumor derived RNA that includes tumor-specific RNA (col. 1, line 46-61). Nair et al. further teach that tumor-specific RNA can be prepared using art-known techniques such as subtractive hybridization against RNA from non-tumor cells to diminish the risk of generating an autoimmune response (col. 2, lines 4-8; col. 3, lines 55-62). Nair et al. also teach that the produced dendritic cells can be used to induce cytotoxic T lymphocytes (CTL) responses or proliferation *in vivo* and *ex vivo*, as well as a method for producing a cytotoxic T lymphocyte by contacting a T lymphocyte *in vitro* with an antigen-presenting cell that is loaded with tumor-derived RNA, and maintaining the T lymphocytes under conditions conducive to CTL proliferation, thereby producing a CTL (col. 2, lines 36-60; col. 6, lines 19-21). Furthermore, Nair et al. teach a method of treating tumor formation in a patient by administering to the patient a therapeutically effective amount of APC loaded with tumor-derived RNA, wherein the APC are derived from the same patient or a matched donor (col. 12, lines 27-34). Additionally, Nair et al. teach that the administration of lymphokines such as IL-2 or IL-4 can also be included in

the CTL and antigen-presenting cells therapies to enhance CTL proliferation (col. 13, lines 2-5).

Since tumor-specific RNA can be prepared using art-known techniques such as subtractive hybridization against RNA from non-tumor cells as taught by Nair et al., the tumor-specific RNA preferentially expressed by tumor cells is selected, and that the preparation of such tumor-specific RNA includes an enriched population containing a plurality of RNA messages preferentially expressed by tumor cells (Please note the definition of "tumor-specific RNA by Nair et al. to be meant an RNA sample that, relative to unfractionated tumor-derived RNA, has a high content of RNA that is preferentially present in a tumor cell compared to a non-tumor cell, col. 3, lines 40-43).

Accordingly, the teachings of Nair et al. meet all the limitation of the instant claims. Therefore, Nair et al. anticipate the presently claimed invention.

Response to Arguments

Applicant's arguments related to the above rejection in the Amendment filed on 1/5/04 (page 8) have been fully considered, but they are not found persuasive.

Applicants argue that the actual examples disclosed by Nair et al. do not describe the use of cytokine such as IL-2 or IL-4. Applicants also argue that there is also no indication of a step of "comparing" first and second nucleic acid sequences, as recited in Applicants' claim 17, to determine sequences preferentially expressed by a target cell population. Applicants further argue that Nair et al. specifically state that practicing the invention "does not require identifying an antigen of the tumor cell or

pathogen" (col. 2, lines 25-27), therefore it is not evident that Nair's disclosure anticipates the presently claimed invention.

Firstly, it is noted that the teachings of Nair et al. are not limited to the actual examples.

Secondly, Nair et al. clearly teach that tumor-specific RNA can be prepared using art-known techniques such as subtractive hybridization against RNA from non-tumor cells, the tumor-specific RNA preferentially expressed by tumor cells is selected, and that the preparation of such tumor-specific RNA includes an enriched population containing a plurality of RNA messages preferentially expressed by tumor cells (Please also note the definition of "tumor-specific RNA by Nair et al. to be meant an RNA sample that, relative to unfractionated tumor-derived RNA, has a high content of RNA that is preferentially present in a tumor cell compared to a non-tumor cell, col. 3, lines 40-58). The step of subtractive hybridization against RNA from non-tumor cells is the step of comparing nucleic acid sequences expressed by a cancer cell population with nucleic acid sequences expressed by a non-cancer cell population.

Thirdly, it is noted that the instant claims do not require that the identity of any tumor antigen has to be identified, simply at least one nucleic acid sequence that is preferentially expressed by a cancer cell population relative to a non-cancer cell population (e.g., there is no need or any requirement that the selected nucleic acid molecule has to be sequenced to reveal its identity to be used in the method as claimed).

Accordingly, amended claims 17-22, 27-29, 32-34, 37 and 39 stand rejected under 35 U.S.C. 102(e) as being anticipated by Nair et al. (U.S. Patent No. 5,853,719) for the reasons already set forth above.

Amended claims 17-22, 27-29, 32-34, 37 and 39 stand rejected under 35 U.S.C. 102(a) as being anticipated by Nair et al. (WO 97/41210) for the same reasons already set forth in the previous Office Action mailed on 7/03/03 (pages 9-11).

With respect to the elected species, Nair et al. (WO 97/41210) teach a method for producing an RNA-loaded antigen-presenting cell (APC) including a dendritic cell by introducing into an APC tumor derived RNA that includes tumor-specific RNA (see abstract). Nair et al. further teach that tumor-specific RNA can be prepared using art-known techniques such as subtractive hybridization against RNA from non-tumor cells to diminish the risk of generating an autoimmune response (page 3, lines 7-12). Nair et al. also teach that the produced dendritic cells can be used to stimulate cytotoxic T lymphocytes (CTL) proliferation *in vivo* and *ex vivo* (page 2, lines 11-14). Nair et al. also teach that if desired, RNA encoding an immunomodulator (e.g., IL-2, IL-1, IL-12) can also be introduced into the APC loaded with tumor-derived RNA to enhance the therapeutic effect of the RNA-loaded APCs (page 4, lines 9-17). Furthermore, Nair et al. teach a method of treating tumor formation in a patient by administering to the patient a therapeutically effective amount of APC loaded with tumor-derived RNA, wherein the APC are derived from the same patient or a matched donor (page 5, lines 18-24). Additionally, Nair et al. teach that the administration of lymphokines such as IL-

2 or IL-4 can also be included in the CTL and antigen-presenting cells therapies to enhance CTL proliferation (page 30, line 33 continues to line 3 of page 31).

Since tumor-specific RNA can be prepared using art-known techniques such as subtractive hybridization against RNA from non-tumor cells as taught by Nair et al., the tumor-specific RNA preferentially expressed by tumor cells is selected, and that the preparation of such tumor-specific RNA includes an enriched population containing a plurality of RNA messages preferentially expressed by tumor cells (Please note the definition of "tumor-specific RNA by Nair et al. to be meant an RNA sample that, relative to unfractionated tumor-derived RNA, has a high content of RNA that is preferentially present in a tumor cell compared to a non-tumor cell, page 8, lines 27-30).

Accordingly, the teachings of Nair et al. (WO 97/41210) meet all the limitation of the instant claims. Therefore, Nair et al. (WO 97/41210) anticipate the presently claimed invention.

Response to Arguments

Applicant's argument related to the above rejection in the Amendment filed on 1/5/04 (page 8) has been fully considered, but it is not found persuasive.

Applicants argue that the PCT does not provide further supports for the rejection based on anticipation under 102(a) for the reasons already discussed for the rejection under 102(e) as being anticipated by Nair et al. (U.S. Patent NO. 5,853,719). Applicants' arguments are respectfully found unpersuasive for the same reasons

already discussed in the Response to Applicants' arguments related to the rejection under 102(e) as being anticipated by Nair et al. (U.S. Patent 5,853,719).

Amended claims 17-20, 23-24, 27-29 and 33 stand rejected under 35 U.S.C. 102(a) as being anticipated by Tuting et al. (J. Immunology 160:1139-1147, 1998) for the same reasons already set forth in the previous Office Action mailed on 7/03/03 (page 11).

Tuting et al. teach a method of preparing autologous human monocyte-derived dendritic cells transfected transiently with plasmid vectors encoding human MART-1/Melan-A, Pmel-17/gp100, tyrosine, MAGE-1 and MAGE-3 by particle bombardment and the transfected dendritic cells were used to stimulate autologous PBMC responder T cells (see abstract, and page 1142, section entitled "Autologous DC transfected with five different melanoma Ag cDNAs elicit Ag- and tumor-reactive CTL *in vitro*").

As the expression plasmids encoding the human melanoma Ags MART-1/Melan-A, Pmel-17/gp100, tyrosine, MAGE-1 and MAGE-3 were selected and utilized by Tuting et al. for transfecting autologous human dendritic cells, comparison nucleic acid sequences expressed by melanoma cells with nucleic acid sequences expressed by non-melanoma cells has been made.

Accordingly, the teachings of Tuting et al. meet all the limitation of the instant claims. Therefore, Tuting et al. anticipate the presently claimed invention.

Response to Arguments

Applicants' argument related to the above rejection in the Amendment filed on 1/5/04 (page 9) has been fully considered, but it is not found persuasive because it appears that Applicants' arguments are directed to a different article of Tuting et al., and not to the article ***Tuting et al. (J. Immunology 160:1139-1147, 1998)***. There are no pages 480-481 in the cited Journal of Immunology. Additionally, the rejected claims do not recite any immunomodulatory factor, let alone IL-2.

Accordingly, amended claims 17-20, 27-29 and 33 stand rejected under 35 U.S.C. 102(a) as being anticipated by Tuting et al. (J. Immunology 160:1139-1147, 1998) for the same reasons set forth above.

Conclusions

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Quang Nguyen, Ph.D., whose telephone number is (571) 272-0776.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's mentor, David Guzo, Ph.D., may be reached at (571) 272-0767, or SPE, Irem Yucel, Ph.D., at (571) 272-0781.

To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1636; Central Fax No. (703) 872-9306.

Quang Nguyen, Ph.D.

DAVID GUZO
PRIMARY EXAMINER